CLAIMS

What is claimed is:

1. A method of making an osteogenic composition, the method comprising:

combining purified collagen, an osteoinductive substance, and water containing dilute acid in a dispersing assembly comprising two vessels and a reduced diameter portion, said vessels being in mutual fluid communication by way of said reduced diameter portion;

forcing said combination from vessel to vessel through said reduced diameter portion a predetermined number of times sufficient to disperse said collagen and osteoinductive substance in said water, such that said collagen is at least partially hydrated and a dispersion is obtained;

allowing said dispersion to stand for a predetermined time interval.

2. The method of claim 1 wherein said dispersing assembly comprises two syringes, each having a plunger, and said step of passing said combination from vessel to vessel comprises sequentially depressing said plungers a predetermined number of times such that said combination is subjected to physical forces sufficient to disperse said collagen and osteoinductive substance in said water, such that said collagen is at least partially hydrated and a dispersion is obtained.

3. The method of claim 1 wherein said predetermined number of passes is up to about 250.

4. The method of claim 1 wherein said step of passing said combination from vessel to vessel comprises:

passing said combination from vessel to vessel a first predetermined number of passes;

allowing said combination to stand for a first predetermined time interval;

passing said combination from vessel to vessel a second predetermined number of passes; and

allowing said combination to stand for a second predetermined time interval, such that a dispersion is obtained.

5. The method of claim 4 wherein said first predetermined number of passes is about 5-150.

6. The method of claim 4 wherein said second predetermined number of passes is about 5-150.

7. The method of claim 4 wherein said first time interval is about 30-60 minutes.

8. The method of claim 4 wherein said second time interval is at least about 12-72 hours.

9. The method of claim 1 wherein said reduced diameter portion comprises a connector and said step of forcing said combination from vessel to vessel through said reduced diameter portion includes passing said combination through said connector.

10. The method of claim 1 further comprising extruding said dispersion to provide an extrudate.

11. The method of claim 10 further comprising molding said extrudate.

12. The method of claim 10 further comprising drying said extrudate to provide a dehydrated osteogenic matrix.

13. The method of claim 12 further comprising sterilizing said dehydrated osteogenic matrix.

14. The method of claim 13 further comprising rehydrating said dehydrated osteogenic matrix.

15. The method of claim 14 further comprising mixing a bulking material with said rehydrated matrix to provide a shapeable osteogenic implant material.

16. The method of claim 15 wherein said bulking material is particulate demineralized bone matrix.

17. The method of claim 15 further comprising shaping said osteogenic implant material.

18. The method of claim 1 wherein said dispersion comprises approximately 1-8% (wt./vol.) collagen.

19. The method of claim 1 wherein said collagen is dehydrated fibrous bovine tendon type I collagen.

20. The method of claim 1 wherein said water containing dilute acid comprises about 10 mM HCl.

21. The method of claim 1 wherein said osteoinductive substance is chosen from the group consisting of bone growth proteins, bone morphogenetic proteins 1-13, osteogenic protein-1 or 2, FGF-I or -II, TGF-beta, GDF-5,6 or 7.

22. The method of claim 1 further comprising combining a biologically active agent other than said osteoinductive substance with said collagen/osteoinductive substance, said agent chosen from the group consisting of growth factors, cartilage inducing factors, angiogenic factors, hormones, antibiotics, antiviral compounds and anticancer compounds.

23. A method of making an osteogenic composition, the method comprising:

combining a predetermined amount of purified collagen, a predetermined amount of an osteoinductive substance, and a predetermined amount of a dilute aqueous acid solution in a dispersing assembly comprising two vessels connected by a reduced diameter portion, said vessels being in mutual fluid communication;

passing said combination from vessel to vessel a predetermined number of times such that said combination is subjected to physical forces sufficient to disperse said collagen and osteoinductive substance in said water, such that said collagen is at least partially hydrated and a thickened dispersion is obtained;

allowing said thickened dispersion to stand for a second predetermined time interval, such that a thick, extrudable dispersion is obtained;

extruding said thick, extrudable dispersion to provide an extrudate; and

drying said extrudate to provide a dehydrated osteogenic matrix.

24. An osteogenic composition comprising a product of the method of claim 1.

25. The osteogenic composition of claim 24 comprising a mixture of purified type I bovine fibrillar tendon collagen and an osteoinductive substance.

26. The osteogenic composition of claim 25 further comprising an active agent other than said osteoinductive substance, said agent chosen from the group consisting of growth factors, cartilage inducing factors, angiogenic factors, hormones, antibiotics, antiviral compounds and anticancer compounds.

27. The osteogenic composition of claim 25 further comprising a bulking material combined with said mixture.

28. The osteogenic composition of claim 27 wherein said bulking material is particulate demineralized bone matrix.

29. The osteogenic composition of claim 25 wherein said osteoinductive substance is chosen from the group consisting of bone growth proteins, bone morphogenetic proteins 1-13, osteogenic protein-1 or 2, FGF-I or -II, TGF-beta, GDF-5,6 or 7.

30. A method of making an implantable osteogenic device comprising:

preparing an osteogenic composition according to the method of claim 10;

dehydrating said extrudate to yield a dehydrated osteogenic product;

rehydrating said dehydrated product;

mixing said rehydrated product with a bulking material to provide a shapeable osteogenic implant material.

31. The method of claim 30 further comprising shaping said osteogenic implant material to provide an implantable osteogenic device.

32. A shaped osteogenic device comprising a product of the method of claim 31.

33. A method of making an implantable osteogenic device comprising:

preparing an osteogenic composition according to the method of claim 10;

dehydrating said extrudate to yield a dehydrated osteogenic product;

rehydrating said dehydrated product;

inserting said rehydrated product into a spinal cage to provide an osteogenic device.

34. An osteogenic spinal cage comprising a product of the method of claim 33.

35. A method of inducing osteogenesis in a subject in need thereof comprising implanting in said subject at a site where osteogenesis is desired a device according to claim 30.

36. The method of claim 35 wherein said site is a dental or periodontal defect site.

37. A method of inducing osteogenesis in a subject in need thereof comprising implanting in said subject in the disk space between two vertebral bodies that are desired to be fused together an osteogenic spinal cage according to claim 34.

38. A kit comprising a predetermined quantity of an osteogenic composition according to claim 25 and a sterility-maintaining cover.

39. The kit of claim 38 further comprising a mixing container.

40. The kit of claim 38 further comprising a predetermined quantity of a bulking material.

41. A method of making a collagenous matrix comprising:

combining collagen and a water containing dilute acid in a dispersing assembly comprising two vessels and a reduced diameter portion, said vessels being in mutual fluid communication by way of said reduced diameter portion;

passing said combination from vessel to vessel a predetermined number of times such that said combination is forced through said reduced diameter portion sufficient to disperse said collagen in said water, such that said collagen is at least partially hydrated and a dispersion is obtained;

allowing said dispersion to stand for a predetermined time interval to yield an extrudable dispersion.

42. The method of claim 41 further comprising molding said extrudable dispersion.

43. The method of claim 41 further comprising dehydrating said dispersion.

44. The method of claim 43 further comprising rehydrating said dehydrated dispersion.

45. The method of claim 44 further comprising mixing a bulking material with said rehydrated dispersion.

46. The method of claim 41 further comprising combining a biologically active agent with said collagen and water.

47. The method of claim 41 wherein said collagen comprises about 1-8 wt% of said dispersion.

48. A collagenous matrix comprising the product of the method of claim 41.

49. A method of administering a biologically active agent to a subject in need thereof comprising:

preparing a delivery vehicle comprising the collagenous matrix of claim 41;

incorporating a biologically active agent into said delivery vehicle; and

implanting said delivery vehicle at a selected site in the body of said subject; and

allowing said biologically active agent to be released from said delivery vehicle at said site.

50. The method of claim 49 wherein said implanting comprises surgical placement of said delivery vehicle.

51. The method of claim 49 wherein said implanting comprises injecting said delivery vehicle.